AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1.   **(currently amended):** A method of performing interactive clinical trials for testing a new drug for cancer related studies, resulting in clinical trial designs, the method comprising:

a)   performing a pre-clinical phase in which a computer model for pharmacodynamics of a drug is determined;

b)   obtaining data to determine the computer model for the pharmacodynamics of the drug of (a) from *in vitro* studies of the effect of the drug in animal cells, and optionally, *in vivo* studies in animals, and obtaining data for the pharmacokinetics of the drug of (a) from *in vivo* studies in animals;

c)   performing a phase I clinical trial in which a clinical trial on at least a single dose of the drug of (a) is administered to at least one human, and the phase I clinical trial is performed in parallel by performing computer simulations using the computer model constructed in step (a);

d)   adjusting the computer model based on comparison of the results of the clinical trial and computer simulations using the computer model, wherein the at least a single dose of step (c) is incrementally increased in at least one dose escalation step[[s]];

e)   calculating the dose escalation step by the computer simulations performed using the computer model in step (d) to obtain a maximal tolerated dose, minimum effective dose, and a recommended dose;

f)   checking the patient ~~drug~~ for cumulative <u>drug</u> effects after administration and providing this information to the computer model;

g)   performing multiple simulations using the computer model with different doses and dosing intervals for different indications and patient populations;

h)   determining, based on step (g) simulations results, an optimal regimen for the most responsive patient populations and clinical indications for a phase II clinical trial;

i)   performing at least one phase II clinical trial where a number of small scale clinical trials are performed in parallel in order to test the optimal treatment regimen from step (h) for different pairs of clinical indications and patient populations;

j)   performing at least one phase III clinical trial for <u>a clinical indication chosen in</u> step (h) ~~chosen clinical indications by~~<u>using a regimen that was chosen in</u> step (i) ~~chosen regimens~~; and

k)   performing at least one phase IV clinical trial<u>, based on, at least, one previous clinical trial,</u> for post-marketing subpopulation analysis <u>that may identify differences in efficacy and toxicity between the subpopulations,</u> and long term product safety assessment.

2.   **(previously presented):** The method of claim 1, wherein in step (c), computer simulations of the model are performed prior to the phase I clinical trial, to predict results of the phase I clinical trial, and the predicted results are compared to the phase I clinical trial results and the computer model is adjusted based on the comparison.

3.   **(previously presented):** The method of claim 1, wherein a first decision whether to continue the phase II clinical trial is made prior to step (i), stopping the trial if an adverse decision is made.

4.   **(previously presented):** The method of claim 1, wherein results of step (h) are used to define clinical indications and define sub-groups of patients most sensitive, susceptible and responsive to the drug.

5.   **(previously presented):** The method of claim 4, wherein an effective treatment regimen is defined for a subset of the subgroups.

6.   **(previously presented):** The method of claim 1, wherein the computer model is adjusted based on whether the clinical trial indicates a result higher than a threshold in at least one of pre-clinical, phase I and phase II trials.

7.   **(previously presented):** The method of claim 1, wherein in step (i), the small clinical trials are performed in parallel for a chosen clinical indication by a chosen treatment regimen.

8.   **(previously presented):** The method of claim 3, wherein in step (j), the most promising trials are chosen for clinical indications most sensitive to the drug administered via the most efficient regimen.

9.   **(previously presented):** The method of claim 8, wherein in step (j), a second decision whether to continue the phase III clinical trial is made, stopping the trial if an adverse decision is made.

10.   **(withdrawn):** The method of claim 9, wherein the second decision is based on a prediction of safety profile of the new drug in the most promising trial compared with safety of pre-existing therapies.

11.   **(previously presented):** The method of claim 9, wherein the decision is based on a prediction of efficacy profile of the drug in the most promising trial compared with efficacy of pre-existing therapies.

12.   **(withdrawn):** The method of claim 1, wherein step (k) is performed to prove safety of the drug.

13.   **(previously presented):** The method of claim 1, wherein step (k) is performed to prove efficacy of the drug.

14.   **(previously presented):** The method of claim 1, when hitherto unknown effects are discovered in step (k), the computer model is adjusted to obtain predictions for new regimens, patient populations and clinical indications.

15.   (currently amended): A method of performing interactive clinical trials for a new drug for cancer related studies, resulting in clinical trial designs, the method comprising a step of administering at least a single dose of a drug *in vitro* or *in vivo* to obtain data ~~from~~ for a pre-clinical phase in which a computer model for pharmacokinetics and pharmacodynamics is created and adjusted based on datafrom *in vitro* studies and optionally *in vivo* studies in animals, wherein the computer model is an in silico patient that is adjusted according to the results of the pre-clinical trials.

16.   (previously presented): A method of performing interactive clinical trials for a new drug for cancer related studies, resulting in clinical trial designs, the method comprising a step of obtaining data from administration of a drug in a dose-escalation during phase I clinical trial performed in parallel with simulated computer predictions, and wherein the simulated computer predictions are compared with clinical results and the comparison is used to adjust the computer model, wherein the computer model is an in silico patient that is adjusted according to the results of the clinical trials.

17.   (previously presented): A method of performing interactive clinical trials for a new drug for cancer related studies, resulting in clinical trial designs, the method comprising: a step of administering at least a single dose of a drug to obtain data to develop a strategy for a phase I clinical trial wherein the phase I clinical trial is performed in parallel with simulated computer predictions, and wherein the simulated computer predictions comprise using a computer model that is an in silico patient that is adjusted according to the results of the clinical trials.

18.   (currently amended): A method of performing interactive clinical trials for a
new drug for cancer related studies, resulting in clinical trial designs, the method comprising a
step of administering at least a single dose of a drug to obtain data ~~from~~ for performing a phase II
clinical trial wherein at least one clinical trial is performed in parallel with- simulations
performed using a computer model, resulting in prediction of one or more trial outcomes,

wherein the prediction of one or more trial outcomes is compared with clinical results
from the phase II clinical trials and the comparison is used to adjust the computer model,
wherein the computer model is an in silico patient that is adjusted according to the results of the
clinical trials.

19.   (currently amended): A method of performing interactive clinical trials for a
new drug for cancer related studies; resulting in clinical trial designs, the method comprising a
step of administering at least a single dose of a drug to obtain data ~~from~~ for performing a phase
III clinical trial in parallel with simulations performed using a computer model that predicts a
better treatment for the design of further clinical trials, resulting in prediction of one or more
trial outcomes,

wherein the prediction is compared with clinical results from the phase III clinical trials
and the comparison is used to adjust the computer model, wherein the computer model is an in
silico patient that is adjusted according to the results of the clinical trials.

20.   (currently amended): A method of performing interactive clinical trials for a
new drug for cancer related studies, resulting in clinical trial designs, the method comprising a
step of administering <u>to a patient</u> at least a single dose of a drug to obtain data ~~from~~for

performing a phase IV clinical trial in parallel with simulations performed using a computer

model that predicts post-marketing efficacy of a drug, and long term drug safety assessment,

resulting in prediction of one or more trial outcomes,

wherein the prediction is compared with clinical results from the phase IV clinical trials

and the comparison is used to adjust the computer model, wherein the computer model is an in

silico patient that is adjusted according to the results of the clinical trials.

21.   (previously presented): The method of Claim 15, wherein the computer model

adjusted according to the results of the pre-clinical trials is used in the design of further pre-

clinical trials.